

REMARKS

Favorable reconsideration of the instant application in view of the following comments is respectfully requested. Claims 4-12 are currently pending. Claims 4-12 have been canceled by the present amendment, and new claims 45-92 are presented herein, to more particularly point out and distinctly claim the subject matter which applicants regard as the invention. Support for these new claims may be found in the specification, for example, as follows:

Support for claim 45 may be found, for example, at page 31, lines 6-34; and for claims 45-47 at page 34, lines 14-21. Support for claim 48 may be found at page 37, line 30, through page 38, line 18; for claims 49 and 50, at page 59, lines 1-9; for claim 51 at page 54, lines 23-25 and elsewhere; for claims 52 and 53 at page 56, line 16 through page 57, line 28. Support for claim 54 may be found at page 36, lines 19-32 and at page 138, line 24 through page 139, line 7. Support for claim 55 may be found at page 33, lines 8-22 and at page 35, section 3. Support for claims 56-58 may be found, for example, at pages 31-32, and in Example 7, including Figures 11 and 12. Support for claims 59-62 may be found at page 93, lines 30-35. Support for claims 60-62 and 67-69 may be found at page 44, line 24 through page 45, line 5. Support for claims 65-66, 70, and 75, may be found at page 40, lines 3-34. Support for claim 71 may be found at page 137, line 35 through page 138, line 4; and support for claim 72 may be found at page 56, lines 5-15. Support for claims 76-80 may be found at page 55, line 1 through page 56, line 4. Support for claims 81-88 may be found at page 87, Section 9; and support for claim 89 may be found at page 40, line 36 through page 41, line 1. Support for claims 90-92 may be found at page 86, line 20 through page 87, line 26.

Applicants' invention is directed to an antibody that comprises an immunoglobulin or an antigen-binding fragment of an immunoglobulin that specifically binds to a Lewis Y membrane antigen of a carcinoma cell, such that upon binding of the antibody to the carcinoma cell, the antibody is capable of being internalized by the cell. As described in the specification and recited in the amended claims, according to certain embodiments the antibody of the invention is also capable of mediating antibody-

dependent cellular cytotoxicity or complement-dependent cytotoxicity. As also described in the specification and recited in the amended claims, according to certain embodiments the antibody may be a polyclonal or a monoclonal antibody or an antigen-binding fragment thereof, or an antibody comprising an immunoglobulin variable region from one species and at least a portion of an immunoglobulin constant region from a second species or an antigen-binding fragment thereof. Applicants respectfully submit that the presently claimed antibody can be prepared readily and without undue experimentation based on the disclosure of the present application and the state of the art.

In certain embodiments the invention is directed to an immunoconjugate that comprises the antibody as described above that is joined to a therapeutic agent, which can be a cytotoxin, an anti-tumor drug, a radioactive agent, a second antibody or an enzyme. In certain other embodiments the invention is directed to an antibody as described above that is a single chain antibody, which in certain further embodiments may be an immunoconjugate as described in the specification and recited in the claims presented herewith by way of amendment. In certain embodiments the invention relates to a recombinant single-chain immunotoxin that comprises a cloned heavy chain Fv portion and a cloned light chain Fv portion derived from a Lewis Y-specific antibody as described above, which portions are joined to a cytotoxic agent. In certain other embodiments the invention is directed to a bifunctional antibody comprising an antibody with two different specificities, one binding specificity for the Lewis Y membrane antigen and the second specificity for a second antigenic site. As also described in the specification and recited in the claims, methods of using an antibody of the subject invention are also provided by the instant application. In certain embodiments, such methods result in selective killing of a tumor cell that expresses the Lewis Y membrane antigen, and in certain other embodiments such methods are used to treat a patient suffering from a malignant disease. The antibody may also be used in a method for imaging a carcinoma cell that expresses the Lewis Y membrane antigen. No new subject matter has been added.

35 U.S.C. § 112, FIRST PARAGRAPH

According to the Action, the Examiner objected to the specification and rejected the claims under U.S.C. § 112, first paragraph, as allegedly failing to provide an adequate written description of the invention and an enabling disclosure. In particular, the Action asserted that the practicability of the invention is unclear where the BR96 antibody is neither structurally characterized nor publicly available, and where the precise BR96 epitope is not defined.

Applicants respectfully traverse this ground for rejection and submit that the rejection is rendered moot in view of the present amendment. More specifically, the new claims presented herewith by amendment do not recite BR96 *per se*, such that applicants submit the invention need not be limited to the particular BR96 antibody that is described in the specification, which is an illustrative example of the claimed invention. In this regard, applicants submit that it is well established that examples are merely illustrative, such that the scope of the claims should not be limited by the scope of the examples.

As noted above, the present invention is directed in part to an antibody that specifically binds to a Lewis Y membrane antigen of a carcinoma cell, and further to the unexpected observation that upon binding of the antibody to the carcinoma cell, the antibody is capable of being internalized by the cell.

The claimed invention is adequately described in the specification as also noted above, including a description of how to make and use the invention. Therefore, applicants respectfully submit that, as provided by the instant application, a person having ordinary skill in the art at the time of filing could readily and without undue experimentation (i) prepare Lewis Y antigen for use as an immunogen to elicit an antibody, for example by using well established chemical methodologies for structurally characterizing Lewis Y antigen and/or determining the presence of Lewis Y antigen on a carcinoma cell surface; (ii) use such a Lewis Y-containing cell or chemical preparation as an immunogen; (iii) screen antibodies elicited by such an immunogen for reactivity with Lewis Y antigen on a carcinoma cell surface; and (iv) secondarily screen positive, Lewis

Y-reactive antibodies for their ability to be internalized by a carcinoma cell upon binding of an antibody to the carcinoma cell surface.

Applicants submit that it is well settled that routine screening does not preclude enablement, and that where, as here, the specification provides a reasonable amount of guidance, even a considerable amount of experimentation is permissible and is not to be regarded as undue experimentation. *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Thus, because the specification combined with the state of the art clearly provides teachings regarding how to obtain an antibody that specifically binds a Lewis Y antigen, and further regarding how to select from among such antibodies an antibody that binds to a Lewis Y antigen on a carcinoma cell surface such that the antibody is internalized, applicants respectfully submit that the amended claims presented herewith comport with the requirements of 35 U.S.C. §112, first paragraph.

35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner rejected claims 4-8 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite because the recited abbreviation "BR96" does not define the properties of the claimed product.

Applicants respectfully traverse this ground for rejection and submit that the rejection is rendered moot where the rejected claims are canceled and the new claims presented herewith by amendment do not recite BR96.

37 C.F.R. 1.75(c)

The Examiner objected to claim 5 under 37 C.F.R. 1.75(c), asserting that the claim was written in improper dependent form. Applicants have requested cancellation of claim 5 and submit that all newly added claims are in proper form as required under 37 C.F.R. 1.75(c).

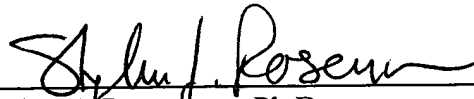
All of the claims remaining in the application are now clearly allowable.
Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Ingegerd Hellstrom et al.

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